Office Action Summary	Application No.	Applicant(s)
	10/593,005	BARDOTTI ET AL.
	Examiner	Art Unit
	OLUWATOSIN OGUNBIYI	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-21* is/are pending in the application.

4a) Of the above claim(s) *14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/21/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendix A*.

Response to Amendment

The amendment filed 3/22/11 has been entered into the record. Claim 12 has been cancelled. Claims 17-18 have been amended. Claims 1-11, 13 and 17-21 are under examination. Claims 14-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/26/10.

Information Disclosure Statement

The information disclosure statement filed 3/21/11 has been considered and an initialed copy is enclosed.

Claim Rejections Withdrawn

The rejection of claims 17 and 18 under 35 U.S.C. 102(b) as being anticipated by Ho et al Vaccine 19 (2001) 716-725 is withdrawn in view of the amendment to the claims.

The rejection of claim 12 under 35 U.S.C. 103(a) as being unpatentable over Ryall et al WO 02/058737 8/1/02 , cited in IDS in view of Ho et al Vaccine 19 (2001) 716-725 is withdrawn in view of the cancellation of the claim.

The rejection of claim 13 under 35 U.S.C. 103(a) as being unpatentable over Ryall et al WO 02/058737 8/1/02, cited in IDS is withdrawn in view of the amendment to the claim.

Claim Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-11 and 19-21 and newly applied to claims 13 and 17-18 under 35 U.S.C. 103(a) as being unpatentable over Ryall et al WO 02/058737 8/1/02 , cited in IDS in view of Ho et al Vaccine 19 (2001) 716-725 and Claus et al. Mol Gen Genet (1997) 257:28-34 is maintained.

Ryall et al in example 6 paragraphs 64-66 teach a method of determining the quantity of each serogroup polysaccharide present in a formulation of a multivalent meningococcal A, C, W-135 and Y capsular polysaccharide diphtheria conjugate vaccine by *component saccharide* analysis using high pH anion-exchange chromatography with pulsed amperometric detection. Thus, the method of Ryall et al inherently analyzes the sialic acid content of the composition (step b), the galactose content of serogroup W135 (step b ii and step c) and the glucose content of serogroup Y (step b iii and step d) . The method of Ryall et al further comprises determining the quantity of protein and the pH of

the vaccine. Ryall et al in example 6 paragraphs 64-66 teach a method comprising manufacturing a vaccine containing a conjugate of a capsular saccharide from serogroup C of Neisseria meningitidis and one or both of: (i) a conjugate of a capsular saccharide from serogroup W135 of Neisseria meningitidis; and/or (ii) a conjugate of a capsular saccharide from serogroup Y of Neisseria meningitidis i.e. the vaccine is a multivalent meningococcal A, C, W-135 and Y capsular polysaccharide diphtheria conjugate vaccine and (b) analyzing the amount of conjugated and/or unconjugated saccharide in the vaccine for each of said capsular saccharides i.e. Ryall et al teach the purity of the multivalent conjugate vaccine is determined by measuring the amount of unbound (unconjugated) polysaccharide in order to determine that the saccharide content is acceptable (determining purity for clinical use, see for example the clinical use in paragraph 75-79)

Ryall et al does not teach (step e) the content of serogroup C saccharide in the composition is determined by comparing the results of sialic acid analysis with the combined results of the glucose and galactose analyses from step b. Ryall et al does not disclose treating the composition in order to depolymerize the capsular saccharides to give their constituent monosaccharides. As to claim 13, Ryall et al does not specifically teach that the vaccine is released for use by physicians. Ryall et al does not disclose the computer apparatus and computer readable storage medium of instant claims 17 and 18.

Ho et al teach the assessment of stability of meningococcal C-CRM 197 glycoconjugate vaccine by measuring the monosaccharide content (sialic acid) using depolymerization (hydrolysis) followed by high pH anion-exchange chromatography with pulsed amperometric detection for measuring sialic acid. See abstract and p. 718 section. 2.4. Ho et al discloses a computer apparatus i.e. a HPAEC-PAD using a BioLC chromatography system with CarboPac PA-1 guard and analytical columns (Dionex, UK) to quantify monosaccharide i.e. sialic acid of meningococcal C-CRM 197 conjugate vaccine and a computer program used to program the runs and data analysis i.e. PeakNet 5.1 software (Dionex) for analyzing the saccharide content of said composition.

Claus et al teach that the capsular saccharide of N. meningitidis serogroup W135 comprises galactose, and that of serogroup Y comprises glucose. See p. 28 column 2.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made that the component saccharide analysis of Ryall et al using high pH anion-exchange chromatography with pulsed amperometric detection would involve depolymerization of the capsular saccharides within the mixture to obtain monosaccharide in order to perform the saccharide analysis using high pH anion-exchange chromatography with pulsed amperometric detection which will quantitate and help one of skill in the art to analyze and compare the different unique monosaccharide structures of each of the capsular saccharides of the different N. meningitidis serotypes i.e. sialic acid for serogroup C, galactose for serogroup W135 and glucose for serogroup Y, thus resulting in the instant invention with a reasonable expectation of success. The motivation to do so is because Ho et al teach that analyzing monosaccharide content of glycoconjugate vaccine using high pH anion-exchange chromatography with pulsed amperometric detection involves depolymerization of the oligosaccharide structure into its subunit before high pH anion-exchange chromatography with pulsed amperometric detection and *Ho et al teach that the reason for quantitating the monosaccharide content of the glycoconjugate vaccine* is to determine the stability and integrity of the vaccine and it would have been prima facie obvious to analyze and compare the monosaccharides unique to each serogroup i.e. sialic acid for serogroup C, galactose for serogroup W135 and glucose for serogroup Y in order to determine the stability and integrity of capsular saccharide of each serotype in the vaccine. As to the limitation, in step e, "the content of serogroup C saccharide in the composition is determined by comparing the results of sialic acid analysis with the combined results of the glucose and galactose analyses from step b", Ryall et al discloses the component saccharide analysis of each serotype including serotype C, and comparing the monosaccharides unique to each serogroup i.e. sialic acid for serogroup C, galactose for serogroup W135 and glucose for serogroup Y in order to determine the stability and integrity of capsular saccharide of each serotype in the vaccine would have been prima facie obvious as Ho teaches that the reason for quantitating the monosaccharide content of the glycoconjugate vaccine is to determine the stability and integrity of the vaccine.

As to claim 13, furthermore, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made that the vaccine manufactured in the steps set forth above and analyzed as set forth in the above rejection is released to physicians. This is because the vaccine was used in a clinical setting and it is reasonably expected that the physicians are present in a clinical setting. MPEP 2141 under "Office Personal as Fact finders" states that: In short, the focus when making a determination of obviousness should be on what a person of ordinary skill in the pertinent art would have known at the time of the invention, and on what such a person would have reasonably expected to have been able to do in view of that knowledge. This is so regardless of whether the source of that knowledge and ability was documentary prior art, general knowledge in the art, or common sense. In the instant case, it is common sense that release of the vaccine and its application in a clinical setting necessarily involves release of the vaccine for use to physicians who would be present in such a clinical setting to, for example, administer the vaccine or monitor the efficacy of the vaccine or diagnose or treat any adverse events in response to the vaccine.

As to claims 17-18, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to automate the process of Ryan and Ho and Claus as combined by using a computer apparatus comprising a computer-readable storage medium storing computer-executable instructions for performing the process steps or by using a computer readable storage medium storing computer executable instructions for analyzing the saccharide content of the composition, the computer executable instructions for (a) receiving data on the sialic acid content and on the glucose and/or galactose content of the sample and calculating from those data the content of capsular saccharide from serogroup C W135 and/or Y. Computer Apparatus and storage medium comprising computer executable instructions for analysis of saccharide content are known in the art: Ho et al discloses a computer apparatus i.e. a HPAEC-PAD using a BioLC chromatography system with CarboPac PA-1 guard and analytical columns (Dionex, UK) and a computer program used to program the runs and data analysis i.e. PeakNet 5.1 software (Dionex) for analyzing the saccharide content of a composition; and thus automating the process of Ryan and Ho and Claus as combined

using computer apparatus comprising computer readable medium storing computer-executable instructions would have been prima facie obvious. Using said computer apparatus and computer readable medium storing computer-executable instructions to automate a known process does not by itself impart nonobviousness to the invention. *In re Venner*, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) and MPEP 2144.04.

Applicants' arguments and the response:

Applicants argue that none of the art identified by the Examiner teaches a process for analyzing the saccharide content of claim 1 (e.g. how to accurately determine the saccharide content of the composition, given that saccharides of serogroup W135, Y and C all contain sialic acid) nor does any of the art recognize the difficulties associated with analyzing the content of the composition of claim 1 as a problem needing to be solved.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., how to accurately determine the saccharide content of the composition, given that saccharides of serogroup W135, Y and C all contain sialic acid) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). For instance the specification on p. 4 lines 1-10 discloses using the difference between sialic acid content and the combined glucose and galactose content to quantify the pre-hydrolysis serogroup c content i.e. the molar amount of serogroup C is calculated according to the molar amount of sialic acid minus the molar amount of (glucose + galactose). If this is the accurate detemination, Applicants are relying upon, this is not recited in the claims.

Applicants argue that the Examiner statement that "it would have been prima facie obvious to analyze and compare the monosaccharides unique to each serogroup i.e. sialic acid for serogroup C, galactose for serogroup W135 and glucose for serogroup Y in order to determine the stability and integrity of capsular saccharide for each serotype of the vaccine" is a conclusory statement and not supported is considered but is not persuasive.

As set forth in the rejection, the motivation to do so is provide by Ho et al who teach that the reason for quantitating the monosaccharide content of the glycoconjugate vaccines is to determine the stability and integrity of the vaccine. Moreover, Ryall et al discloses a method of determining the quantity of each serogroup polysaccharide present in a formulation of a multivalent meningococcal A, C, W-135 and Y capsular polysaccharide diphtheria conjugate vaccine by *component saccharide* analysis. Thus, based on the teachings of Ryall et al and Ho et al, one of ordinary skill in the art at the time the instant invention was made would have analyzed and compared the monosaccharides unique to each serogroup i.e. sialic acid for serogroup C, galactose for serogroup W135 and glucose for serogroup Y in order to determine the stability and integrity of capsular saccharide for each serotype of the vaccine.

Applicants argue that contrary to the Examiner's assertion, the content of serogroup C saccharide in the composition of claim 1 cannot be accurately determined just by analyzing sialic acid content of the composition, because sialic acid is not unique to serogroup C saccharides – it also occurs in saccharides of serogroup W135 and Y and the obviousness analysis fails to include step(e) as presently claimed. Applicants' arguments are considered but are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the content of serogroup C saccharide in the composition of being accurately determined) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Claim 1 in step b comprises a step of analyzing the sialic acid content of the composition. In claim 1 step e, "the content of serogroup C saccharide in the composition is determined by comparing the results of sialic acid analysis with the combined results of the glucose and galactose analyses from step b". There is no requirement for accurate determination of the content of serogroup C saccharide in the composition – the claim recites "*comparing* the results of sialic acid analysis with the combined results of the glucose and galactose analyses from step b". Claim 1 merely "compares sialic acid analysis with the combined results of the glucose and galactose

analyses from step b". The scope of "comparing" is broad and in the instant case and for this rejection is interpreted to mean considering the quantity of the sialic acid analysis with the quantity of the glucose and galactose analysis. There is no recitation in the claims of any calculations to be made to arrive at the accurate sialic acid content due to the presence of serogroup C in the composition. USPTO personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). Limitations appearing in the specification but not recited in the claim should not be read into the claim. *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted "in view of the specification" without importing limitations from the specification into the claims unnecessarily). *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969). See also *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320,1322 (Fed. Cir. 1989) ("During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow.... The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed.... An essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous. Only in this way can uncertainties of claim scope be removed, as much as possible, during
the administrative process."). See MPEP 2106 (II)(C). For the reasons above, the rejection is maintained.

New Claim Objections/Rejections

Claim Objections

Claim 17 is objected to as being dependent on a cancelled claim (claim 12). Please amend claim 17 to remove dependency on claim 12.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 17 and 18 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The broadest reasonable interpretation of a claim drawn to a computer readable medium typically covers forms of non-transitory tangible media and transitory propagating signals per se in view of the ordinary and customary meaning of computer readable media. See MPEP 2111.01. See OG notice 1351 OG 212 2/23/10 (attached as Appendix A). To overcome the rejection, Applicants may amend the claims by adding the limitation "non-transitory" to the claims. See directive in OG notice 1351 OG 212 2/23/10.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 13, and 17-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are “vague and indefinite” in view of the recitation of “the content of serogroup C saccharide in the composition is determined by comparing the results of sialic acid analysis with the combined results of the glucose and galactose analyses from step b”. It is not clear in the claim exactly how the content of serogroup C saccharide in the composition is determined by comparison of the results of sialic acid analysis with the combined results of the glucose and galactose analyses from step b. “Comparing” is a broad term and the metes and bounds of “comparing' is not set forth in the specification. The term "comparing" in step e of claim 1 is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree. It is suggested that

Applicants amend step e of claim 1 to particularly point out and distinctly claim exactly how the content of serogroup C saccharide in the composition is determined. The specification on page 4 lines 8-10 discloses subtraction of the molar glucose and galactose content from the molar sialic acid content to obtain the sialic acid from serogroup C and reciting in the claim will obviate this issue.

Status of Claims

Claims 1-11, 13, and 17-21 are rejected. No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is (571)272-9939. The examiner can normally be reached on M-F 8:30 am- 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Oluwatosin Ogunbiyi/
Primary Examiner, Art Unit 1645